Pursuant to 37 CFR 1.121(c)(1)(ii), a marked up version of the claims showing the changes made appears as Appendix B of this Amendment.

REMARKS

Applicant has amended the claims so as to clarify and more particularly indicate the claimed subject matter, and to better indicate that the claimed subject matter is to the novel and unobvious peptides of the invention. No new matter is added. The amendment is made for the sole purpose of expediting prosecution.

Claims 1-18, 31-34, 43-44, 46-47, 49-55 and 57-60 are in the case. The Examiner withdrew claims 5, 43-44, 46-47, 49-55, and 57-60 as drawn to a non-elected invention. As such, claims 1-4, 6-18, 31-34, 39, 45, 48 and 61 are under examination, with the species corresponding to SEQ ID NO: 18 elected.

Drawings

The Examiner objected to the specification since the reference to Figure 10 did not refer to Figures 10A and 10B. This has been corrected in this response.

Written Description

Rejection of Claims 1-3, 7, 8-18, 31-34 and 39 under 35 U.S.C. §112, first paragraph

The Examiner rejected claims 1-3, 7, 8-18, 31-34 and 39 under 35 U.S.C. §112, first paragraph. The specification was said to not contain a written description of the invention in full, clear, concise and exact terms/sufficient detail to allow one of ordinary skill in the art to conclude Applicants had possession of the claimed invention. Specifically, the Examiner said that despite Applicants' arguments in their February 20, 2002 response, the specification failed to provide an adequate written description of such "homologs, analogs or derivatives" of the claimed peptides. The Examiner said that homologs are "usually naturally occurring molecules (having) a defined structure which cannot be predicted based on the structure provided in Applicants' specification; that one could not predict which allelic forms or alternative amino acid substitutions might be. As such, the Examiner argued that the claims were defined by function without "any" recitation of structure and the specification therefore lacked a proper written description. Applicants traverse in view of the amendments herein and the comments below.

Applicants have amended the claims to expedite prosecution. The amended claims, *e.g.*, claim 1 and claim 12, more particularly point out the claimed purified leptin peptides have sequences selected from the novel small peptides disclosed in Applicants' specification, *e.g.*, SEQ ID NO: 18. Claim 4 has been amended to more particularly point out that the claimed leptin peptide has leptin or leptin-like activity, and that its sequence consists essentially of the amino acid sequence Xaa_n-Ser-Cys-Xaa_1-Leu-Pro-Xaa_2-Xaa_3-Xaa_n.

The present amendment makes it clearer that Applicants are in possession of the claimed invention. Applicants' disclose the claimed sequences, their utility and their activity. At the very least one of ordinary skill in the art may routinely make the protein of the elected species, SEQ ID NO: 18 (as well as the other sequences not presently under consideration) on a protein synthesizer with the sequence information. One of ordinary skill in the art would be able to make or recognize homologs to the claimed peptides - whether or not the homologs are naturally occurring - since the claimed structures disclosed in the specification, are precise enough to be able to determine the percent homology, and/or determine whether the peptides have leptin or leptin-like activity. Derivatives (and analogs) of the claimed peptides are, similarly, clearly outlined:

> *... may be full length or other than full length, if said derivative or analog contains a modified nucleic acid or amino acid... Derivatives or analogs of the aforementioned peptides include... molecules comprising regions that are substantially homologous to the aforementioned peptides... (page 20, line 19) Derivatives of the aforementioned peptides may be produced by alteration of their sequences by substitutions, additions or deletions that result in functionally-equivalent molecules. ... In another specific embodiment, one or more amino acid residues within the sequence of interest may be substituted by another amino acid of a similar polarity and net charge, thus resulting in a silent alteration. Substitutes for an amino acid within the sequence may be selected from other members of the class to which the amino acid belongs. For example, nonpolar (hydrophobic) amino acids include alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan and methionine. Polar neutral amino acids include glycine, serine, threonine, cysteine, tyrosine, asparagine, and glutamine. Positively charged (basic) amino acids include arginine, lysine and histidine. Negatively charged (acidic) amino acids include aspartic acid and glutamic acid. (page 25, line 26, to page 26, line 5.)*

One of ordinary skill in the art knows that modifications to peptides such as derivatization and substitution are done on a routine basis, for a number of reasons. Applicants accordingly are not obligated to demonstrate or present all possible embodiments of the invention, *e.g.*, derivatized or substituted species. Applicants are entitled to draft their claims as broad as the prior art allows.

Lastly, Applicants understand that the claimed fragments of the peptides of the invention are not rejected by the Examiner.

The claimed peptides are fully described by Applicants' specification, and in a way that one of ordinary skill in the art will understand. As such, and in view of the amendments

presented herein, the rejected claims are submitted to be patentable under 35 U.S.C. §112, first paragraph, and withdrawal of the rejection is in order and is respectfully requested.

Enablement

Rejection of Claims 1-4, 6-18, 31-34, 39, 45, 48, 56 and 61under 35 U.S.C. §112, first paragraph

The Examiner rejected claims 1-4, 6-18, 31-34, 39, 45, 48, 56 and 61 under 35 U.S.C. §112, first paragraph, as containing subject matter not adequately described in the specification so as to enable one of ordinary skill in the art to make and/or use the invention. Applicants appreciate the recognition that the specification is enabling for leptin fragments containing SEQ ID NOs: 2 or 18, but traverse the part of the rejection that argues the specification is not enabling for modified peptides, *e.g.*, % homologs, substituted peptides, and derivatives.

The Examiner alleged that a "substantial amount of experimental trial and error in the form of deletional and substitutional analysis to identify those critical residues" would be needed to produce a mutant of the disclosed peptide, thus "clearly" constituting undue experimentation. As noted above in Applicants' response to the Written Description rejection, however, the specification does provides proper and sufficient enabling support for substituted and derivatized peptides.

In view of the claim amendments and Applicants' comments, it is respectfully submitted that they properly and sufficiently address the Examiner's concerns. As such, the rejection has been overcome, and Applicants request withdrawal of the rejection.

SUMMARY

On the basis of the foregoing amendments, Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact either of the undersigned at the telephone number provided below.

Respectfully submitted,

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Appendix A: marked up version of the specification sh wing the changes made

In the Specification:

Replace the paragraph beginning at page 11, line 12, with the following:

FIGs. 10A and 10B ~~is a~~are graphic representations of the effects of 12 daily injections of LEP(116-130) synthetic peptide on body weight gain and food consumption in female *db/db* mice.

Appendix B: marked up versi n of the claims sh wing the changes made

1. (Amended twice) A purified leptin peptide ≤ 15 amino acids long, having a sequence selected from the group consisting of SEQ ID NOS: 2-10 and 18, and fragments, homologs, analogs and derivatives thereof which retain activity of the native sequence, wherein ~~the~~ said peptide has the following characteristics:

(a) it is a substantially homogenous preparation; ~~and~~

(b) it has at least ~~70~~80% homology to any one of the sequences ~~set forth in~~ of SEQ ID NOS: 2-10 and 18, and ~~wherein~~

(c) ~~the~~ said leptin peptide modulates body mass.

4. (Amended three times) A leptin peptide ~~having~~ consisting essentially of the amino acid sequence Xaa_n-Ser-Cys-Xaa_1-Leu-Pro-Xaa_2-Xaa_3-Xaa_n, wherein:

(a) either Xaa_n is zero or a contiguous stretch of at most seven peptide residues derived from SEQ ID NOS: 1 or 17; and

(b) Xaa_1, Xaa_2 and Xaa_3 is any amino acid substitution;

wherein said leptin peptide has leptin or leptin-like activity.

12. (Amended three times) A peptide ~~comprising~~ consisting essentially of an amino acid sequence of the leptin protein of any one of SEQ ID NOS:1 and 17, and selected from the group consisting of:

(i) a sequence comprising amino acids 21-35 (SEQ ID NO:3);

(ii) a sequence comprising amino acids 31-45 (SEQ ID NO:4);

(iii) a sequence comprising amino acids 41-55 (SEQ ID NO:5);

(iv) a sequence comprising amino acids 51-65 (SEQ ID NO:6);

(v) a sequence comprising amino acids 61-75 (SEQ ID NO:7);

(vi) a sequence comprising amino acids 71-85 (SEQ ID NO:8);

(vii) a sequence comprising amino acids 81-95 (SEQ ID NO:9);

(viii) a sequence comprising amino acids 91-105 (SEQ ID NO:10);

(ix) a sequence comprising mouse amino acids 116-122 (SEQ ID NO:2);

(x) a sequence comprising human amino acids 116-122 (SEQ ID NO:18);

and fragments, derivatives, homologs and analogs thereof.

61. (amended once) A purified peptide comprising the amino acid residues sequence of SEQ ID NO:18.